Oral opiates and respiratory function

SIR,—In the course of Dr A M Hoy's comments (20 March, p 898) on Dr J D J Havard's leading article (27 February, p 612) he quoted a case report to support the view that the respiratory depressant effect of morphine is reduced provided oral morphine dosage is titrated against a patient's level of pain.¹ There is more substantive supportive evidence from a prospective study, a preliminary report of which appeared elsewhere.² This study is now complete (paper in preparation), and there is no evidence that chronic ventilatory failure is either common or severe in persons with severe pain from advanced cancer given oral morphine (in individual doses four-hourly) with dosage titrated against the level of pain. This is true in patients who are pain-free with significant amounts of morphine in their plasma³ and in those with active respiratory tract disease—for example, carcinoma of the bronchus. Indeed, used in this fashion, oral opiates may have little clinically significant effect on respiratory function, and given correctly seem unlikely to cause death by respiratory depression.

Thus given good practice the concern that relief of pain may shorten life seems misplaced—indeed, experienced physicians often comment on the manner in which patients "bounce back" once pain from malignancy has been adequately controlled. Perhaps it is time the profession established widely what is good medical practice in an area plagued by myths and misunderstandings.

T D WALSH

St Christopher's Hospice,
London SE26 6DZ

¹ Hanks GW, Twycross RG, Lloyd JL. *Anaesthesia* 1981;**36**:37-9.

² Walsh TD, Baxter R, Bowman KB, Leber B. *Pain* 1981; suppl No 1:S39.

³ Grabinski PY, Kaiko RF, Walsh TD, Foley M, Houde R. *J Pharm Sci* (in press).

Survival and desferrioxamine in thalassaemia major

SIR,—Dr B Modell and colleagues (10 April, p 1081) show a relation between increasing dosage of desferrioxamine treatment and improved survival in patients with thalassaemia major, suggesting that treatment prevented disease due to iron overload. It would have been useful to have been given some information as to the number of patients receiving vitamin C supplements since vitamin C has important effects on iron metabolism.

These effects were initially evaluated following observations on the Bantu tribesmen, who were found to have dietary haemosiderosis and nutritional vitamin C deficiency.¹ Despite a high total body iron load they appeared relatively immune from the harmful effects of the excess iron. Histologically the iron was found to be deposited primarily in reticulo-endothelial cells, as opposed to the predominant parenchymal distribution of idiopathic haemochromatosis.² The Bantu were frequently found to have low serum iron concentrations which increased when vitamin C therapy was given. Observations on scorbutic guinea pigs have confirmed the mobilising effect of vitamin C on storage iron deposits.³

Cohen *et al*⁴ reported on the surprisingly good clinical condition of a 26-year-old patient with thalassaemia major and vitamin C deficiency. Following two episodes of clinical scurvy the patient was treated with 100 mg

vitamin C daily. This resulted in a dramatic increase in the serum iron and ferritin concentrations, which had been relatively low considering the transfusion history. It was suggested that, as in the Bantu, vitamin C deficiency appeared to confer some protection from iron-induced tissue damage.

In patients with iron overload from repeated transfusions the concentration of vitamin C in white cells is frequently reduced because of the rapid conversion of the vitamin to oxalic acid.⁵ The urinary iron excretion mediated by desferrioxamine, however, is greatly enhanced by vitamin C therapy.⁶ Hence, many patients currently receiving regular desferrioxamine are also receiving vitamin C supplements in order to ensure that they are ascorbate-replete. What then happens to the apparent protective effect of vitamin C deficiency? In fact vitamin C therapy may be positively harmful. Serial echocardiographic studies demonstrated a fall in ejection fraction and dilation of the heart in eight out of 11 patients with thalassaemia major shortly after vitamin C therapy.⁷ Left ventricular function improved in six patients when therapy was withdrawn. Iron is thought to damage tissues by peroxidation of membrane lipids and this effect is augmented *in vitro* by vitamin C.⁸ In addition the mobilisation of iron stores manifest by the striking increase in serum iron with vitamin C may mean that iron is redistributed from reticuloendothelial to parenchymal cells.

Hence, the survival of patients with thalassaemia major treated with desferrioxamine needs to be related to the vitamin C state. Is the beneficial effect of vitamin C deficiency outweighed by improved iron excretion with vitamin C repletion or does a fine balance exist? The establishment of the optimal vitamin C state may well constitute one of the "general improvements in ancillary management," which the authors refer to, and could, therefore, "yield improved survival mistakenly attributed to infusions of desferrioxamine."

J A MURRAY

Royal Hallamshire Hospital,
Sheffield S10 2JF

¹ Seftel HC, Malkin C, Schmaman A, *et al*. *Br Med J* 1966;**i**:642-6.

² Bothwell TH, Abrahams C, Bradlow BA, Charlton RW. *Arch Pathol* 1965;**79**:163-8.

³ Lipschitz DA, Bothwell TH, Seftel HC, Wapnick AA, Charlton RW. *Br J Haematol* 1971;**20**:155-63.

⁴ Cohen A, Cohen IJ, Schwartz E. *N Engl J Med* 1981;**304**:158-60.

⁵ Wapnick AA, Lyndi SR, Krawitz P, Seftel HC, Charlton RW, Bothwell TH. *Br Med J* 1968;**iii**:704-7.

⁶ O'Brien RT. *Ann NY Acad Sci* 1974;**232**:221-5.

⁷ Henry W. *Ann Intern Med* 1979;**91**:892-4.

⁸ Wills ED. *Biochem Pharmacol* 1972;**21**:239-47.

Intraspinal opiates and itching: a new reflex?

SIR,—Drs P V Scott and H B J Fischer (3 April, p 1015) propose a theory to explain the high incidence of facial itching that they have observed following the administration of intraspinal opiates. They suggest that the phenomenon is probably unrelated to the opiate-induced histamine release and that it may result from an enkephalinergic reflex with central relays in the medulla closely linked to the spinal nucleus of the trigeminal nerve. They also suggest that the addition of local anaesthetic to the opiate solution may prevent itching by blocking this spinal reflex.

Nasal itching is, of course, a recognised side effect of systemic morphine administration.

Following spinal opiate administration facial itching, particularly of the nose, has often been reported¹⁻⁶ but is not as common as generalised itching^{1,5,7} or itching of a more segmental nature, usually confined to the dermatome involved in the analgesia.^{2,4,5,7-9} The site of itching may differ between patients receiving the same drug. The reported incidence varies from 0% to 100% between different trials, and itching has been recorded following morphine, pethidine, methadone, diamorphine, hydromorphone, and fentanyl. Preservative has been implicated as a possible cause⁹ but is not used with pethidine, methadone, diamorphine, or fentanyl.

Intrathecal morphine produces the highest incidence of itching,^{1,6} and obstetric patients seem to be most at risk whatever the drug. The problem occurs least frequently in patients with chronic pain. A rash has only been described in one patient though antihistamines have been reported as effective treatment by some^{5,10} and ineffective by others.⁷

In our experience using epidural fentanyl in labour, itching has occurred in 20-25% of individuals and is almost always experienced in the lower abdomen and thighs. It was never described as severe or troublesome as in some other trials.³ In all our cases the fentanyl was administered with a small dose of bupivacaine. Using a similar mixture, also in obstetrics, Desprats⁴ reported a 70% incidence of pruritus, sometimes facial. So we cannot agree with Dr Scott and Dr Fischer that the addition of local anaesthetic eliminates the itching.

It is characteristic of research into spinal opiates that results from different centres using similar techniques vary widely. We do not believe, however, that the theory suggested by Dr Scott and Dr Fischer can explain the itching phenomenon fully, but the true aetiology eludes us.

D M JUSTINS
FELICITY REYNOLDS

Anaesthetic Unit,
St Thomas's Hospital Medical
School,
London SE1 7EH

¹ Baraka A, Noueihid R, Hajj S. *Anesthesiol* 1981;**54**:136-40.

² Barron DW, Strong JE. *Anaesthesia* 1981;**36**:937-41.

³ Booker PD, Bryson THL, Beddard J. *Anaesthesia* 1980;**35**:377-9.

⁴ Desprats R, Mar B, Grandjean H, Pontonnier G. *Anaesthesia* 1982;**37**:500.

⁵ Rawal N, Sjostrand U, Dahlstrom B. *Anesth Analg* 1981;**60**:726-31.

⁶ Scott PV, Bowen FE, Cartwright P, *et al*. *Br Med J* 1980;**281**:351-3.

⁷ Reiz S, Westberg M. *Lancet* 1980;**ii**:203-4.

⁸ Justins DM, Francis D, Houlton PG, Reynolds F. *Br J Anaesth* (in press).

⁹ Torda TA, Pybus DA. *Anaesth Intens Care* 1981;**9**:129.

¹⁰ Weddel SJ, Ritter RR. *Anesthesiol* 1981;**54**:210-4.

Injuries incurred at "roller discos"

SIR,—I read with interest Mr A J Wilkinson's paper (17 April, p 1163) on "roller disco" injuries. We are in the process of studying these injuries in our accident and emergency department. Our figures as yet are small, but if representative we would see approximately 100 skaters a year, 40% with a fracture. The user rate in the Edinburgh "roller disco" is roughly 100 000 a year. So, in fact, the injury rate is 1 per 1000 skaters, making the sport, in my eyes, very safe.

The role of protective gear is unknown; certainly it is rarely used—perhaps more important is the quality of the skates themselves. There is wide variation in the standard of skates available, and it remains to be seen